Lichen Planus Pemphigoides in a Patient After Combination Ipilimumab and Nivolumab Therapy

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Published In/Presented At

Oberlender, S, Mitton, M. (2019, March 22). *Lichen Planus Pemphigoides in a Patient After Combination Ipilimumab and Nivolumab Therapy*. Poster Presented at: The Philadelphia Dermatological Society Meeting. Philadelphia, PA.

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HISTORY OF PRESENT ILLNESS: 61 year-old Hispanic male presents with a one-month history of a diffuse rash with associated altered mental status, pain and pruritus. At the onset of the rash patient was undergoing treatment with ipilimumab and nivolumab for cT4NxM1a (stage IV) adenocarcinoma of the lung with metastasis to the ipsilateral lung and mediastinum. The patient completed four cycles before stopping therapy due to an inpatient psychiatric hospitalization. Thirty-to-sixty days after his last immunotherapy cycle, he developed a diffuse rash which continued to worsen, prompting dermatology evaluation.

MEDICAL/SURGICAL HISTORY: Stage IV adenocarcinoma of the lung, stage 3 CKD, bipolar disorder with suicidal ideations, CAD, Type II DM, HTN, cirrhosis, diastolic CHF, previous alcohol abuse

MEDICATIONS: Amlodipine, aspirin, atorvastatin, cholecalciferol, folic acid, furosemide, gabapentin, hydroxyzine, insulin, isosorbide mononitrate, melatonin, mupirocin, oxcarbazepine, prednisone, prochlorperazine, propranolol, quetiapine, thiamine

PREVIOUS TREATMENTS: Methylprednisolone 1mg/kg BID, eight-week prednisone taper beginning at 60mg BID

PHYSICAL EXAMINATION: Diffuse hemorrhagic crusted plaques on upper and lower lips. Multiple necrotic, black, crusted, pink-red papules and plaques on chest, back, upper extremities, and thighs, worse on extensor and weight-bearing areas. Occasional non-blanching, pink papules noted on central back and right thigh. Multiple, bleeding ulcerations with violaceous borders on sacral region and buttocks.

LABORATORY DATA: Glucose 316mg/dL (65-99), Cr 2.0mg/dL (0.53-1.30), Na 127mmol/L (135-145), Albumin 2.8g/dL (3.5-4.8), AST 62U/L (<41), GFR 35mL/min/1.73m2 (>60), PT 16.6 sec (12-14.6), NT-proBNP 839pg/mL (<125), CBC, remaining CMP all WNL.

STUDIES: CT chest, abdomen and pelvis on 11/2018 showed multiple small pulmonary nodules are stable to slightly decreased in size since previous exam.

Figure 1: Erosions and crusted lesions of LPP

Figure 2: Lichen planus lesions with hemorrhage

Figure 3: Mucosal involvement of LPP

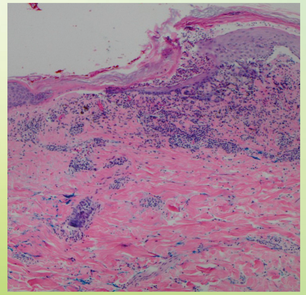

Figure 4: H&E highlighting lichen planus changes with dermo-epidermal clefting and eosinophils

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BIOPSY: *Health Network Laboratories* (S18-50470, 11/10/18) Central back and right thigh: "interface dermatitis with eosinophils; superficial impetiginization."

Mayo Medical Laboratories (S18-50470, 11/10/18) Central back DIF: "continuous strong linear deposition of IgG and C3 along the BMZ. Scattered and clumped cytoids of IgM and IgA in the papillary dermis. Continuous strong shaggy deposition of fibrinogen along the BMZ."

Lichen planus pemphigoides is an autoimmune disease that is thought to be a combination of lichen planus and bullous pemphigoid. It is initiated by lichen planus causing damage to the epidermis and dermoepidermal junction which releases hidden antigens. These antigens lead to circulating IgG antibodies against portions of the basement membrane. The most common antibody is against the MCW-4 epitope of the NC16A4 domain of BPAg2, but several others have been reported.

Lichen planus pemphigoides is characterized by bullous lesions appearing within previous lichen planus sites as well as on normal skin. Histopathologically, both H&E and DIF of the lesions will either show evidence of lichen planus, bullous pemphigoid or a combination of the two.

There are several associations reported with lichen planus pemphigoides. Many cases are idiopathic, but medications such as ACE inhibitors, simvastatin, PD-1 inhibitors, and antituberculous drugs as well as PUVA, sun exposure, pregnancy, and, rarely, malignancy have also been reported as causes.

Therapy with immune checkpoint inhibitors, such as PD-1, PD-L1, and CTLA-4 inhibitors, is a rare cause of lichen planus pemphigoides, but commonly causes cutaneous toxicity. The most common manifestations are pruritus and a morbilliform eruption. However, lichenoid reactions, psoriasis, acneiform eruptions, vitiligo, sarcoidosis, bullous pemphigoid, dermatomyositis, and alopecia areata have also been reported. While each medication has the propensity for this toxicity by itself, combination CTLA-4 and PD-1 inhibitors have been implicated in the development of earlier, more frequent and more severe reactions.

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